US009192314B2

(12) United States Patent
McLaughlin et al.

(10) Patent No.: US 9,192,314 B2
(45) Date of Patent: Nov. 24, 2015

(54) **PROBE FOR NEURAL RECORDING AND OPTICAL SPECTROSCOPIC INTERROGATION**

(75) Inventors: **Bryan McLaughlin**, Cambridge, MA (US); **John LeBlanc**, North Andover, MA (US)

(73) Assignee: **The Charles Stark Draper Laboratory, Inc.**, Cambridge, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 766 days.

(21) Appl. No.: **13/434,313**

(22) Filed: **Mar. 29, 2012**

(65) **Prior Publication Data**

US 2012/0287420 A1 Nov. 15, 2012

Related U.S. Application Data

(60) Provisional application No. 61/468,842, filed on Mar. 29, 2011.

(51) **Int. Cl.**

A61B 5/0478	(2006.01)
A61B 5/04	(2006.01)
A61B 5/00	(2006.01)
A61N 5/06	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 5/04001*** (2013.01); ***A61B 5/0084*** (2013.01); ***A61B 5/6848*** (2013.01); ***A61B 5/6868*** (2013.01); ***A61N 5/0622*** (2013.01); *A61B 2562/0233* (2013.01); *A61B 2562/046* (2013.01); *A61B 2562/12* (2013.01); *A61B 2562/226* (2013.01); *A61B 2562/227* (2013.01)

(58) **Field of Classification Search**

CPC A61B 5/0084; A61B 5/0086; A61B 5/04001; A61B 5/0478; A61B 5/0484; A61B 5/40; A61B 5/4041; A61B 5/4058–5/407; A61B 5/4893; A61B 5/6846; A61B 5/6847; A61B 5/6848; A61B 5/6868; A61B 5/6877; A61B 2562/0238; A61B 2562/0233; A61B 2562/066

USPC 600/373, 377, 378

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,048,359	A *	4/2000	Biel	.... 607/92
2002/0045832	A1	4/2002	Giller et al.	

(Continued)

FOREIGN PATENT DOCUMENTS

WO WO-2011068696 A2 6/2011

OTHER PUBLICATIONS

A New Class of Chronic Recording Multichannel Neural Probes With Post-Implant Self-Deployed Satellite Recording Sites; Daniel Egert and Khalil Najafi, WIMS; Univ. of Michigan, (2011).

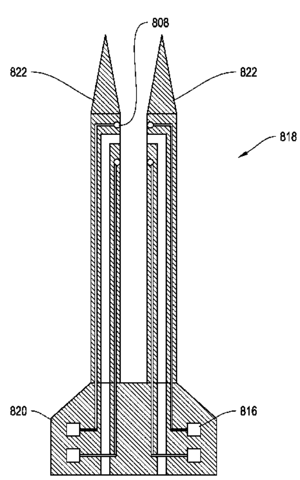
(Continued)

Primary Examiner — Linda Dvorak
Assistant Examiner — Erin M Cardinal
(74) *Attorney, Agent, or Firm* — Edward A. Gordon; Foley & Lardner LLP

(57) **ABSTRACT**

In various embodiments, a probe includes at least one shank, optical components disposed within the shank for transmitting light into a sample and collecting light from the sample, and electrical components disposed within the shank for recording an electrical signal from the sample. In certain embodiments, a method includes collecting light from the sample using a first shank of the probe, recording an electrical signal from the sample using a second shank of the probe, and analyzing the collected light and the electrical signal.

12 Claims, 13 Drawing Sheets



(56) **References Cited**

U.S. PATENT DOCUMENTS

2003/0091289	A1*	5/2003	Saito et al.	385/49
2004/0006274	A1*	1/2004	Giller et al.	600/473
2008/0077200	A1*	3/2008	Bendett et al.	607/89
2009/0118800	A1	5/2009	Deisseroth et al.	
2009/0177144	A1	7/2009	Masmanidis et al.	
2009/0210039	A1*	8/2009	Boyden et al.	607/89
2010/0016732	A1	1/2010	Wells et al.	
2010/0022861	A1*	1/2010	Cinbis et al.	600/325
2011/0024771	A1	2/2011	Hajj-Hassan et al.	
2011/0060377	A1	3/2011	Howard	
2011/0106206	A1	5/2011	Schiff	
2011/0112591	A1	5/2011	Seymour et al.	
2011/0208031	A1	8/2011	Wolfe et al.	
2011/0295331	A1	12/2011	Wells et al.	
2011/0295347	A1*	12/2011	Wells et al.	607/89
2012/0035583	A1	2/2012	Sepkuty	
2012/0089205	A1*	4/2012	Boyden et al.	607/88
2013/0030274	A1*	1/2013	Jamieson et al.	600/377

OTHER PUBLICATIONS

A Microprobe with Integrated Amplifiers for Neurophysiology; K.D. Wise and J. B. Angell; Session IX: Integrated Electronics in Biomedicine; THAM 9.1; ISSCC 71 Stanford Univ., CA., (1971).

On the Design of Multi-Site Microelectrodes for Neuronal Recordings; U. G. Hofmann, et al.; Micro Tec 2000, Hanover, Germany.

Hajj-Hassan Metal: Brain machine interfaces combining microelectrode arrays with nanostructured optical biochemical sensors II. Proceedings of the SPIE—The International Society for Optical Engineering SPIE—The International Society for Optical Engineering USA, vol. 7188, 2009, XP002676682.

Il-Joo Cho et al: "A 16-site neural probe integrated with a waveguide for optical stimulation". 23rd IEEE International Conference on Micro Electro Mechanical Systems (MEMS 2010) IEEE Piscataway, NJ, USA, 2010, pp. 995-998, XP002676681.

International Search Report in PCT/US2012/031232 dated Jun. 11, 2012.

Royer Sebastien et al: "Multi-array silicon probes with integrated optical fibers: light-assisted perturbation and recording of local neural circuits in the behaving animal." The European Journal of Neuroscience Jun. 2010 LNKD-PUBMED:20529127, vol. 31, No. 12, Jun. 2010, pp. 2279-2291, XP002676683.

Zhang J et al: "A microelectrode array incorporating an optical waveguide device for stimulation and spatiotemporal electrical recording of neural activity". Proceedings of the 31st Annual International Conference of the IEEE Engineering in Medicine and Biology Society: Engineering the Future of Biomedicine, EMBC 2009—Proceedings of the 31st Annual International Conference of the IEEE Engineering in Med, 2009, pp. 2046-2049, XP002676680.

* cited by examiner

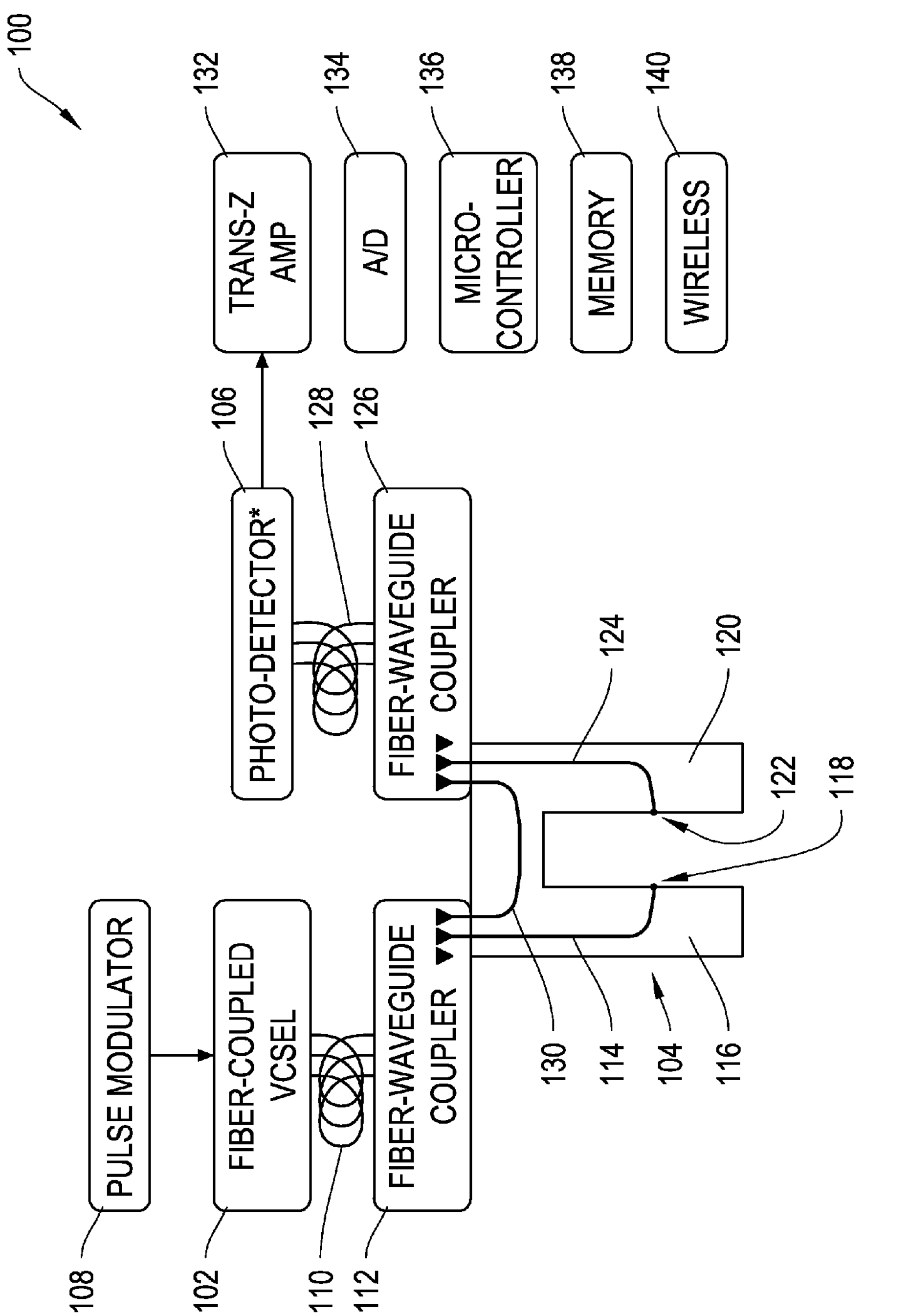

100
TRANS-Z AMP
132
A/D
134
MICRO-CONTROLLER
136
MEMORY
138
WIRELESS
140
PHOTO-DETECTOR*
106
128
126
FIBER-WAVEGUIDE COUPLER
124
120
122
118
PULSE MODULATOR
FIBER-COUPLED VCSEL
FIBER-WAVEGUIDE COUPLER
130
114
104
116
108
102
110
112

FIG. 1

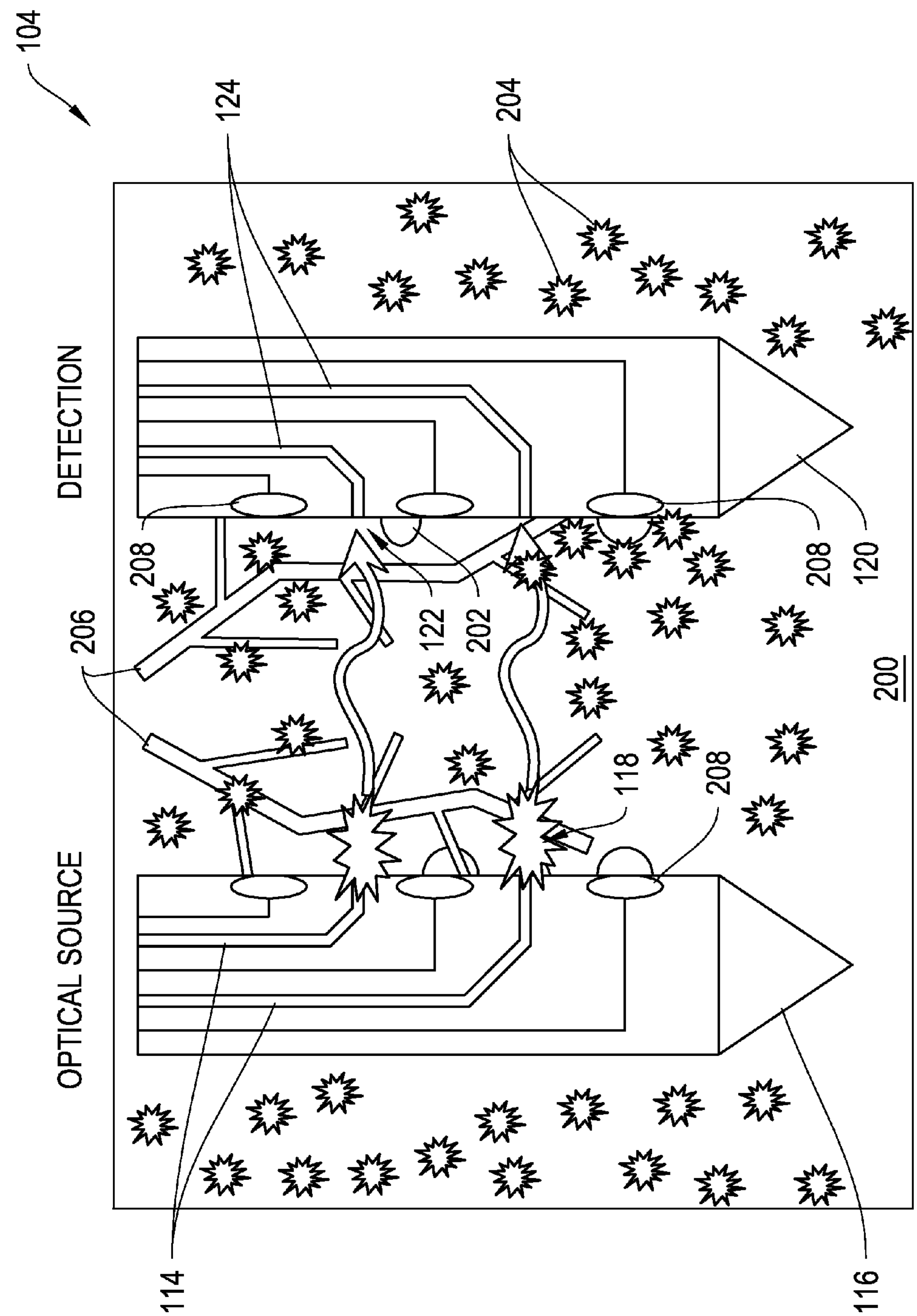

104
DETECTION
OPTICAL SOURCE
124
204
208
206
122
202
208
120
200
118
208
114
116

FIG. 2

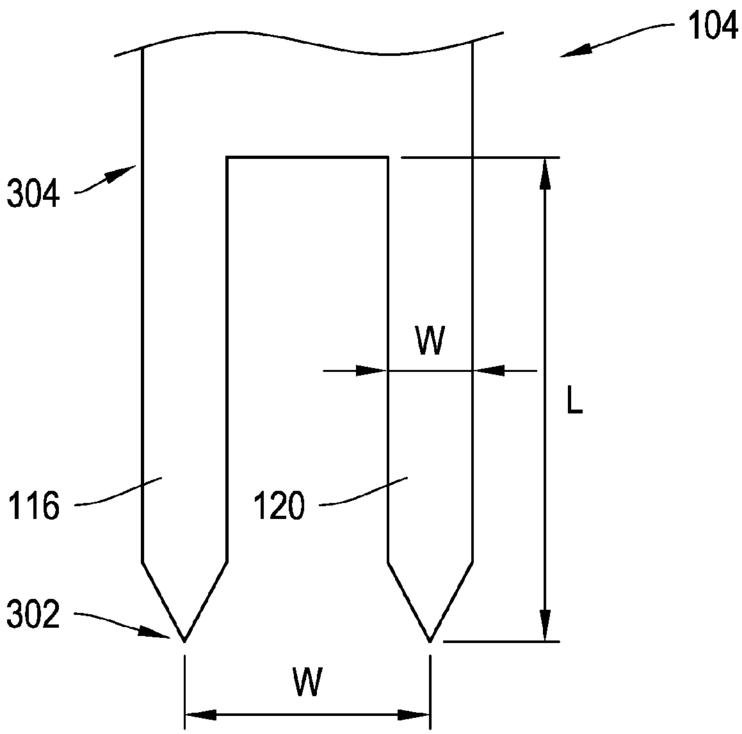


FIG. 3a

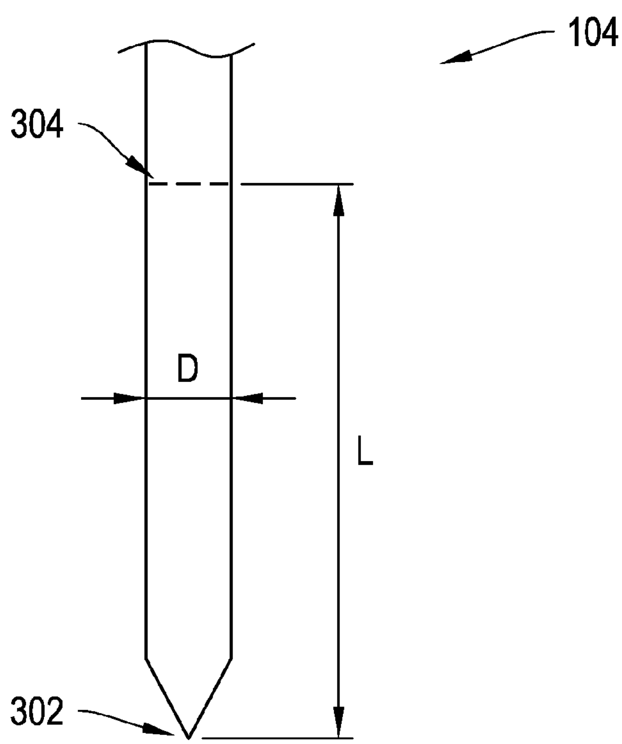


FIG. 3b

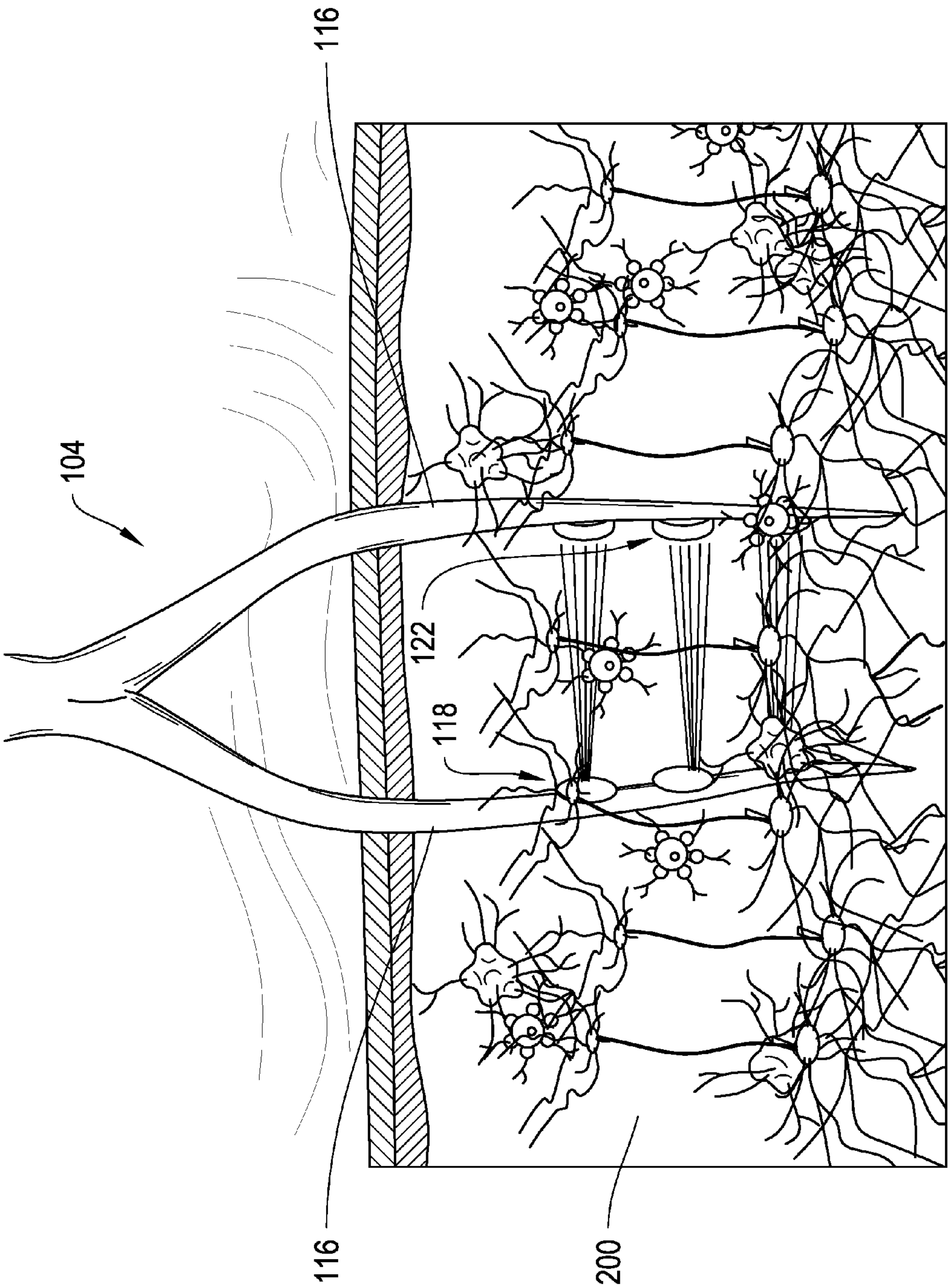


FIG. 4

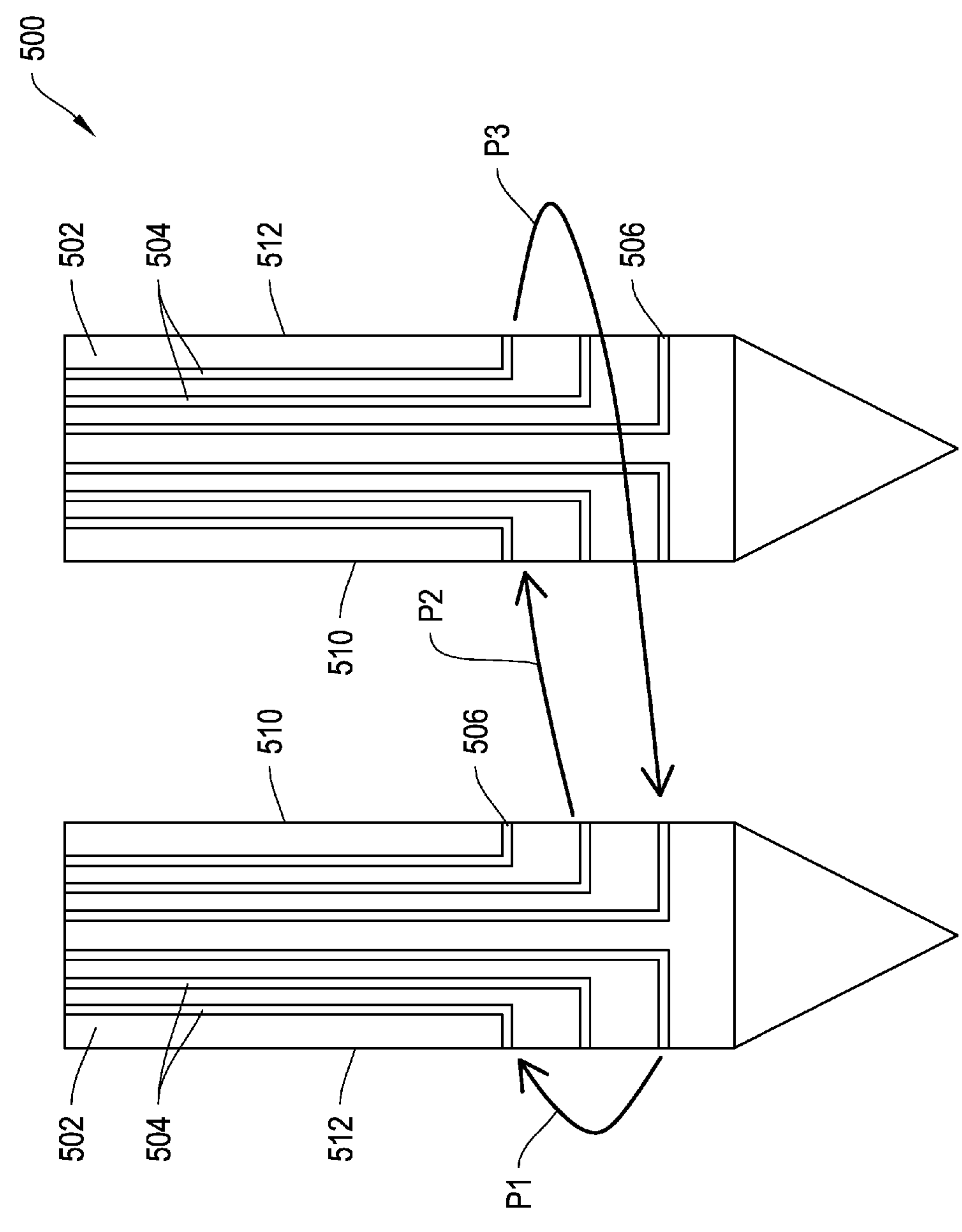


FIG. 5

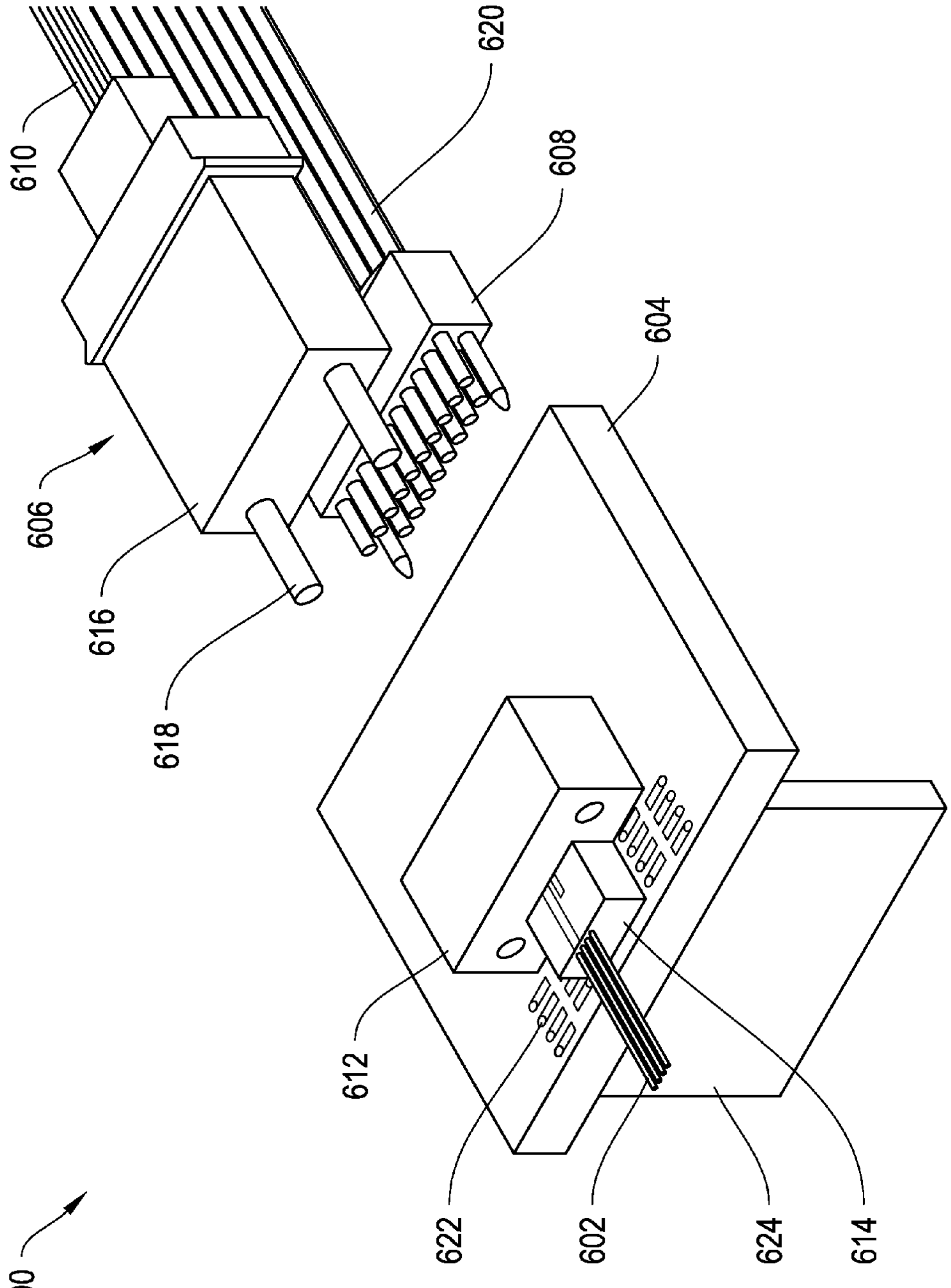


FIG. 6

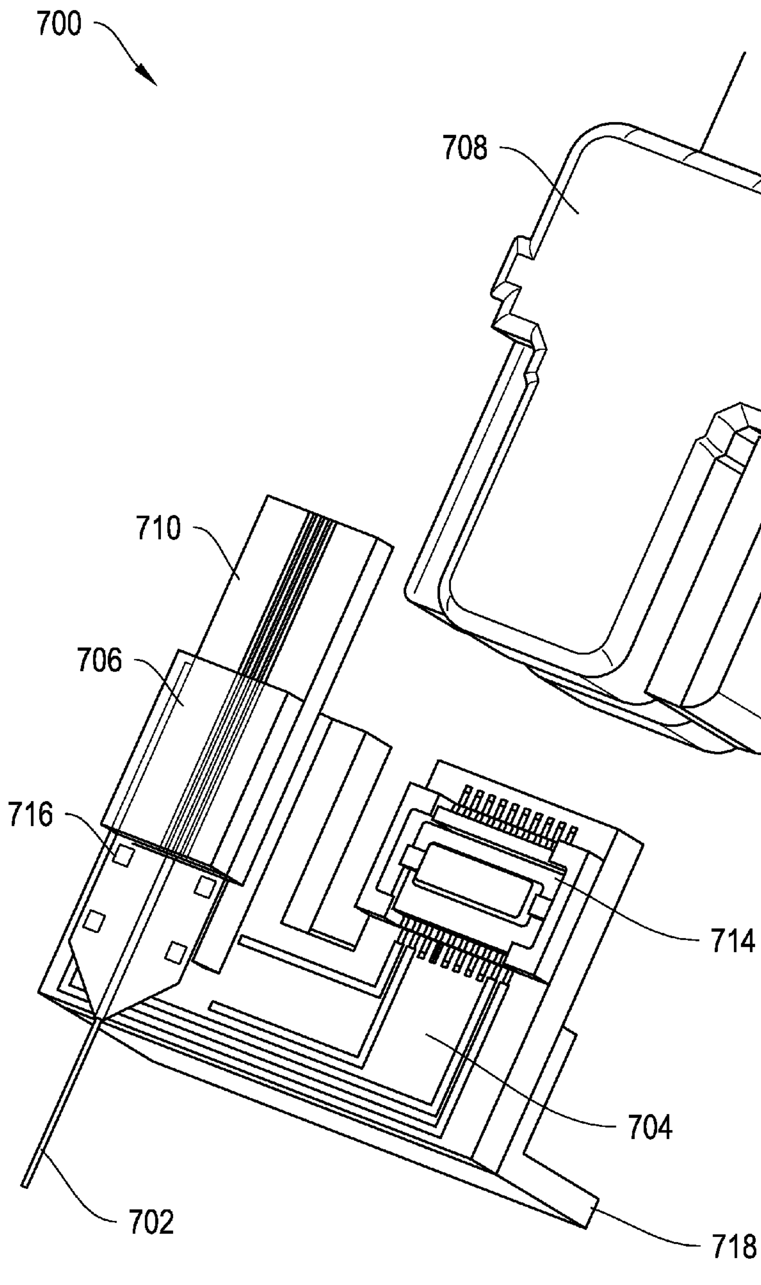


FIG. 7

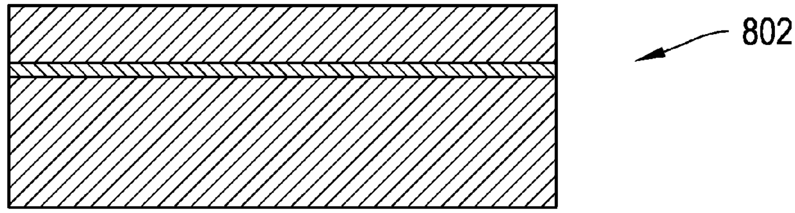


FIG. 8a

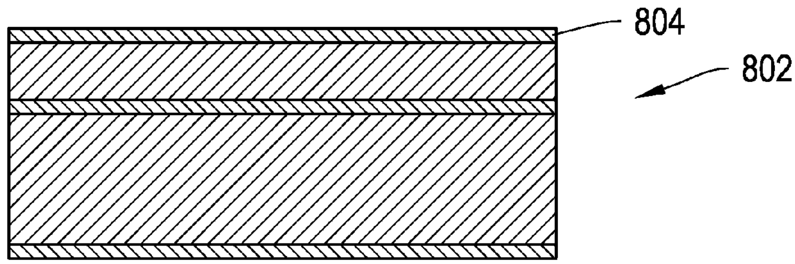


FIG. 8b

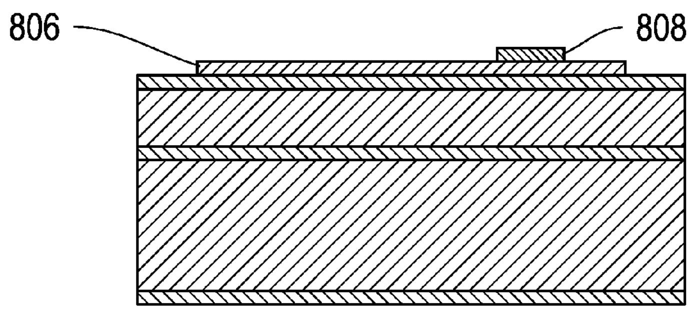


FIG. 8c

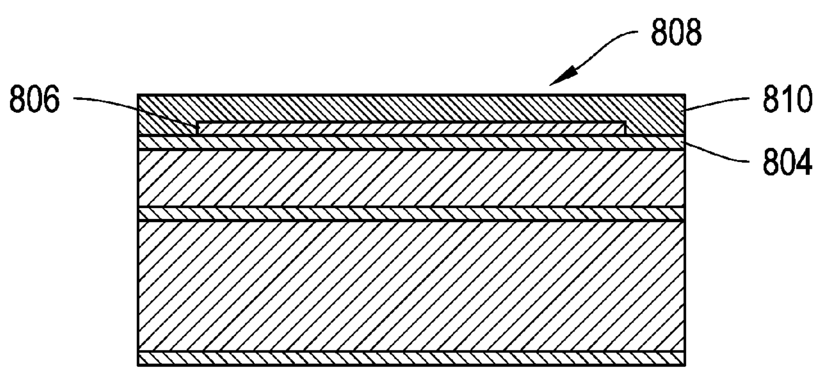


FIG. 8d

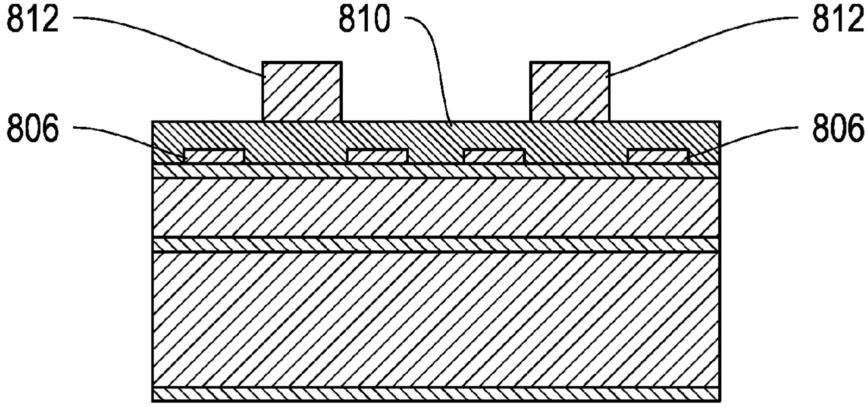


FIG. 8e

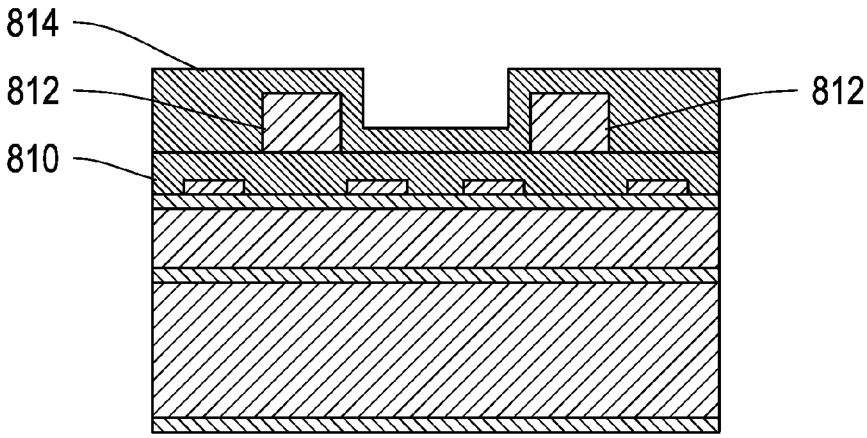


FIG. 8f

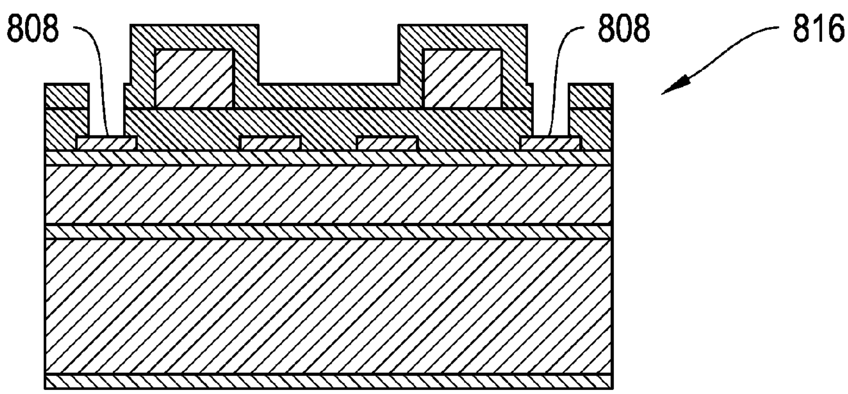


FIG. 8g

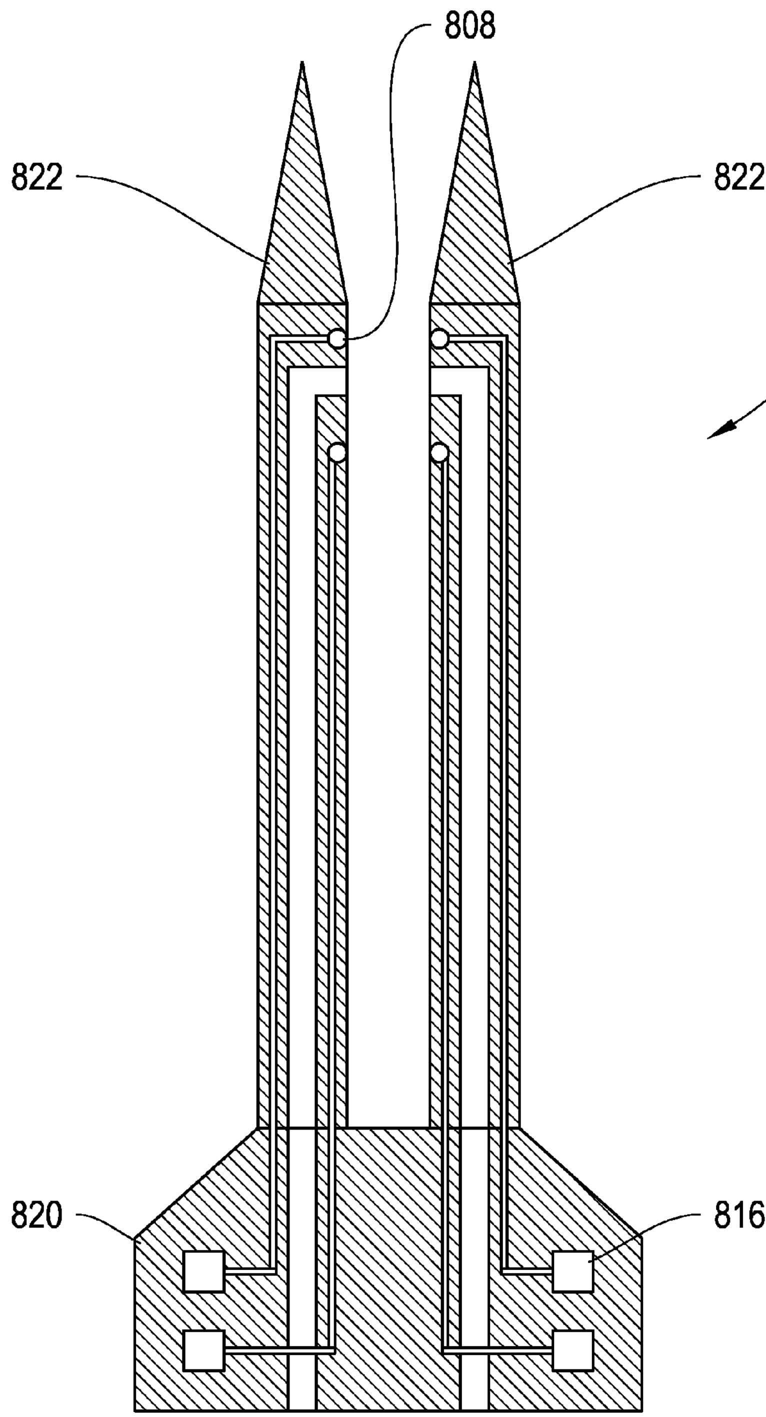


FIG. 8h

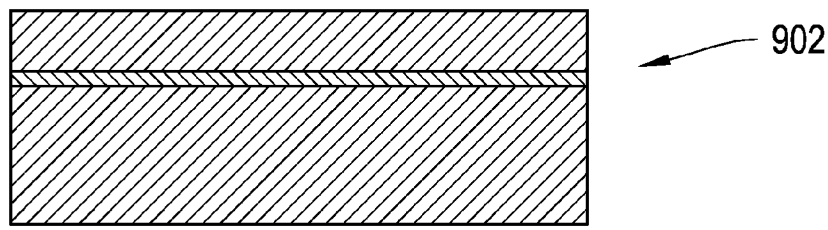


FIG. 9a

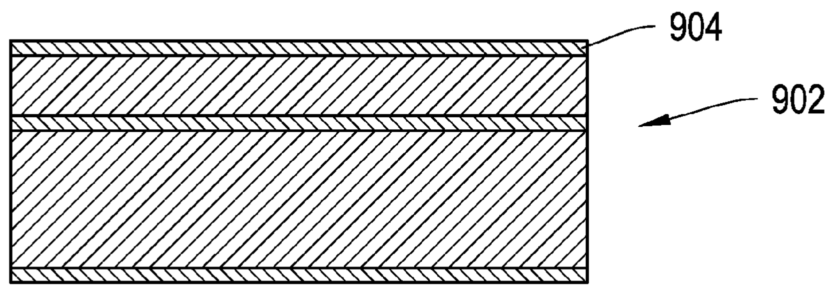


FIG. 9b

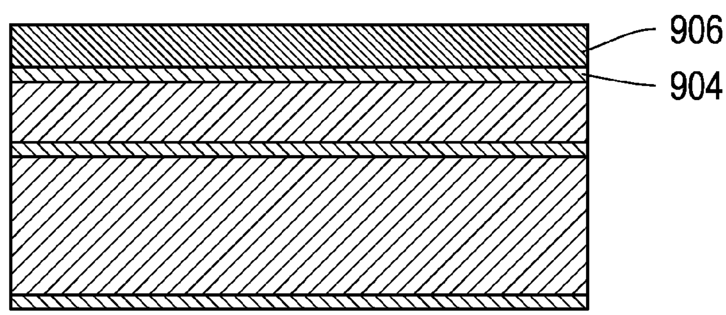


FIG. 9c

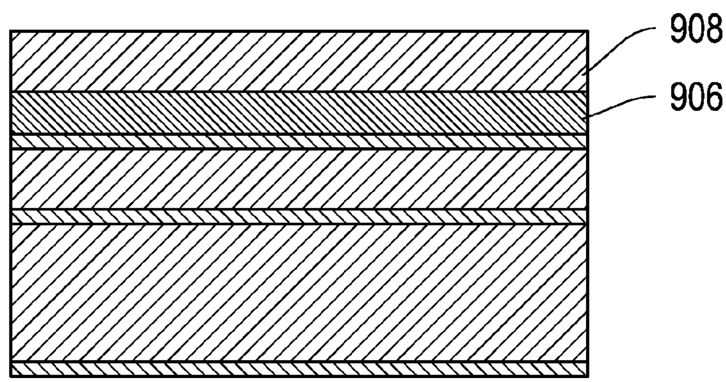


FIG. 9d

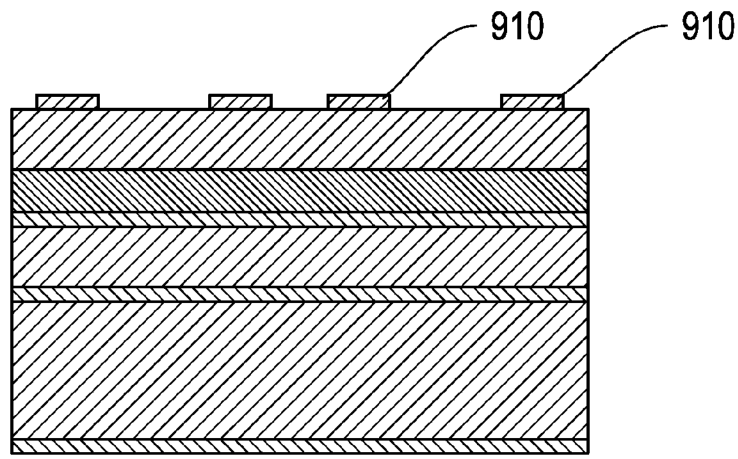


FIG. 9e

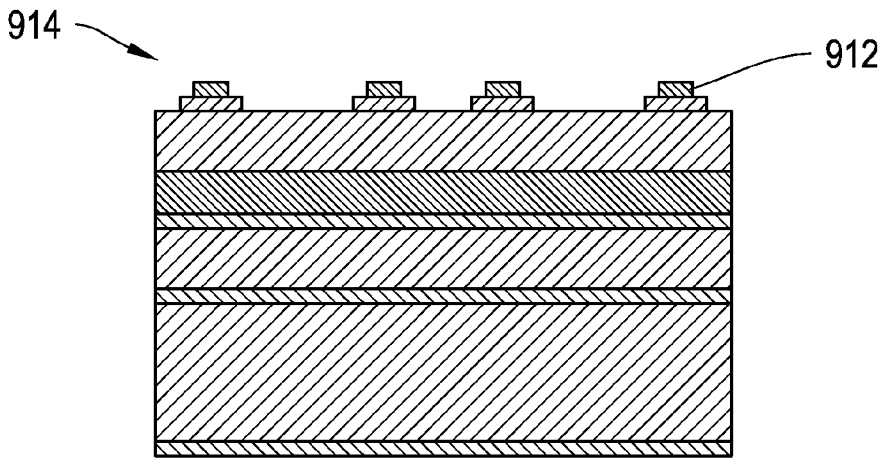


FIG. 9f

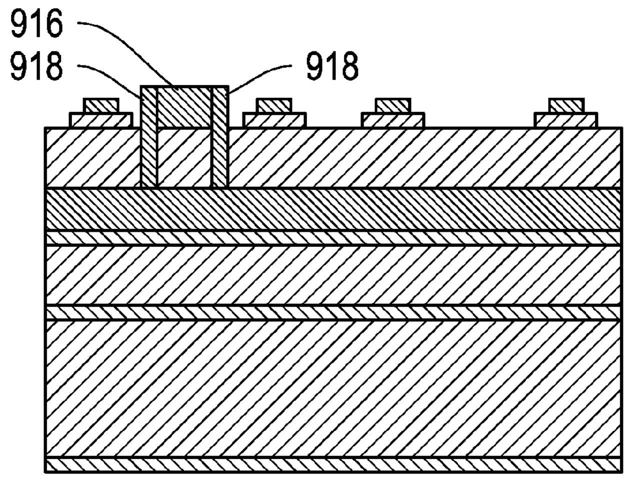


FIG. 9g

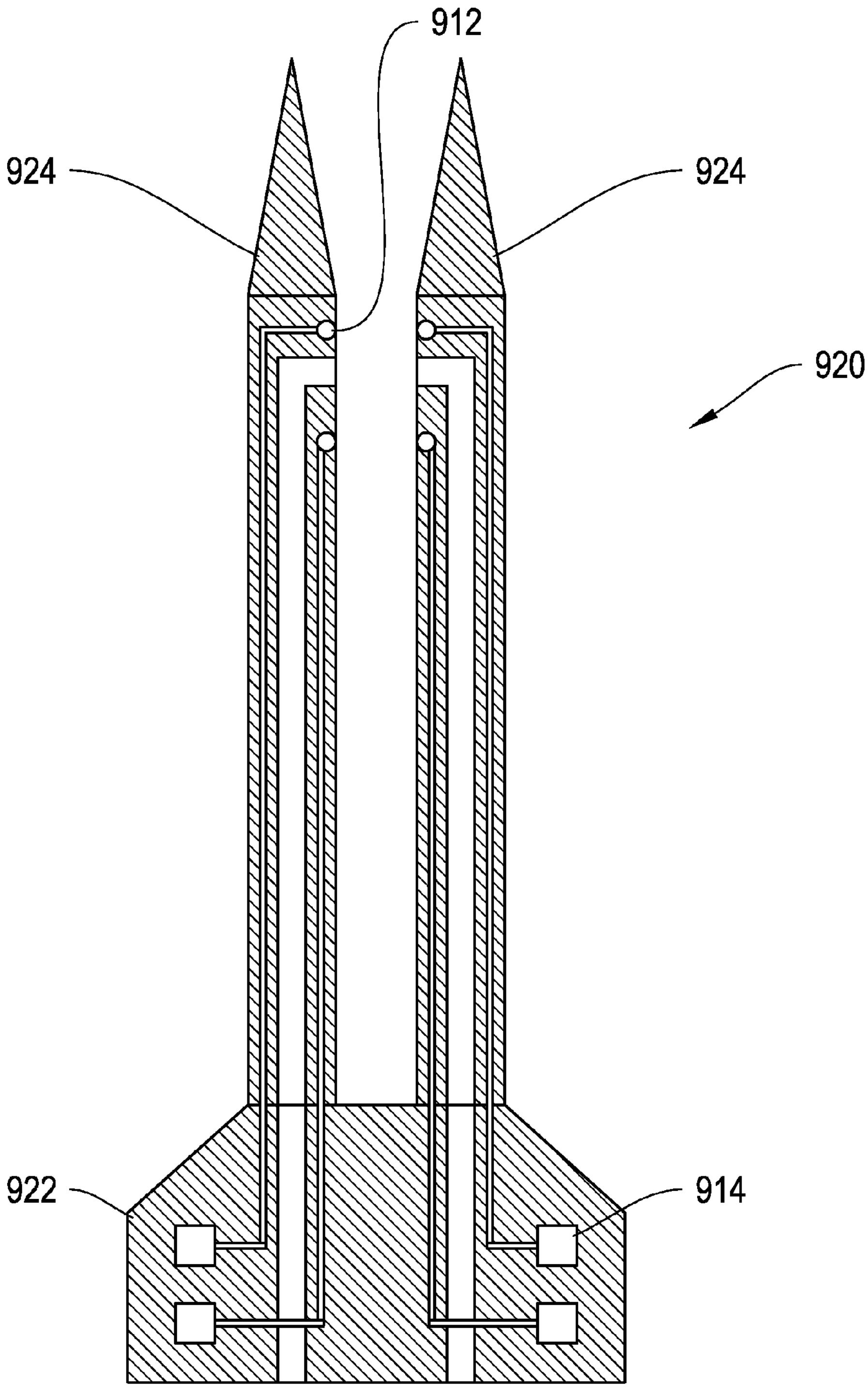


FIG. 9h

PROBE FOR NEURAL RECORDING AND OPTICAL SPECTROSCOPIC INTERROGATION

CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority to and the benefit of, and incorporates herein by reference in its entirety, U.S. Provisional Patent Application No. 61/468,842, which was filed on Mar. 29, 2011.

TECHNICAL FIELD

In various embodiments, the invention relates to devices for stimulating and recording bioelectrical and optical spectroscopic activity. In particular, embodiments of the invention relate to small-scale, implantable probes for electrically and/or optically stimulating and recording neural activity.

BACKGROUND

Electrical stimulation and recordation of neural tissue may be performed by implanting into the tissue a device that includes an electrical lead having one or more electrodes. Typically, the lead is coupled to a signal generator that delivers electrical energy through the electrodes to the neural tissue, thereby stimulating an increase, decrease, or block of neuronal activity. The electrical response of the neural tissue may be measured and recorded.

Optical techniques may also be used for stimulating, monitoring, inhibiting, and/or modulating neural activity. Photostimulation, for example, may include various modes of interaction between light and the target neurons, including a variety of photo-physical and photo-biochemical effects, with various intrinsic components or exogenous sensitizers.

Devices for such purposes have received increasing attention from researchers and clinicians, especially as biomaterials and the technology of microscale probes and electronics have improved. Existing devices, however, are incapable of performing a desired combination of optical and electrical interrogation and/or recordation. Further, implantation of such devices may cause tissue damage and scar tissue buildup, which existing devices and methods are incapable of adequately detecting and monitoring.

Accordingly, there is a need for an improved, small-scale neurological device for electrically and/or optically stimulating and recording neural activity.

SUMMARY OF THE INVENTION

In various embodiments, the present invention features a probe or optrode for optically and electrically stimulating and recording neural activity. The optrode achieves this by combining optical components (e.g., waveguides) with electrical components (e.g., recording electrodes) in a single probe. For example, the optrode may include an optical waveguide embedded within an electrode substrate. The configuration allows the probe to provide optical spectroscopic interrogation and optical spectroscopic collection, in addition to neural recordation and/or bioimpedance measurements. In various embodiments, optical measurements are performed to monitor tissue damage and scar tissue buildup that may occur during and following implantation of the optrode. The optrode has a wide-range of biological applications, including, for example, treatment of Parkinson's disease, epilepsy, depression, obesity, hypertension, and heart disease. The optrode may also be used for cortical recording studies, for example, involving brain-computer-interfaces.

In general, in one aspect, embodiments of the invention relate to a probe. The probe includes at least one shank, optical components disposed within the at least one shank, and electrical components (e.g., an electrode) disposed within the at least one shank. The optical components are for transmitting light into a sample (e.g., neural tissue) and/or collecting light from the sample. The electrical components are for recording an electrical signal from the sample.

In certain embodiments, the optical components include at least one waveguide for transmitting light through the at least one shank. The waveguide may include, for example, a photodefinable polymer. In one embodiment, the optical components are in optical communication with one or more apertures defined by the at least one shank. In various embodiments, the electrical components are configured to apply a voltage to the sample and detect an electrical response of the sample. A width and a depth of the at least one shank is each preferably between about 10 microns and about 100 microns. For example, the width may be about 25 microns and the depth may be about 10 microns. In some embodiments, the at least one shank includes two shanks. A separation distance between the two shanks is preferably between about 20 microns and about 1000 microns (e.g., about 100 microns, or about 200 microns).

In general, in another aspect, embodiments of the invention relate to a system. The system includes a light source, a probe, a photo-detector, and a plurality of waveguides (e.g., external waveguides). The waveguides are for transmitting light from the light source to the probe and from the probe to the photo-detector. The probe includes at least one shank, optical components disposed within the at least one shank, and electrical components disposed within the at least one shank. The optical components are for transmitting light into a sample and collecting light from the sample. The electrical components are for recording an electrical signal from the sample. In certain embodiments, the electrical components are further configured to apply a voltage to the sample and detect an electrical response of the sample.

In general, in another aspect, embodiments of the invention relate to a method. The method includes collecting light from a sample, recording an electrical signal from the sample, and analyzing the optical characteristics of the collected light and the electrical signal to determine a health of the sample and/or neural activity within the sample. The light is collected using an optical component that is disposed within a first shank of a probe. The electrical signal is recorded using an electrical component that is disposed within a second shank of the probe.

In certain embodiments, the first and second shanks are the same shank or different shanks. The recording step may include detecting an electrical response to an applied voltage.

These and other objects, along with advantages and features of the embodiments of the present invention herein disclosed, will become more apparent through reference to the following description, the accompanying drawings, and the claims. Furthermore, it is to be understood that the features of the various embodiments described herein are not mutually exclusive and can exist in various combinations and permutations.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention. In the following description, various embodiments of the present invention are described with reference to the following drawings, in which:

FIG. **1** is a schematic view of an optrode system, in accordance with one embodiment of the invention;

FIG. **2** is a schematic front view of an optrode inserted into cortical neural tissue, in accordance with one embodiment of the invention;

FIG. **3***a* is a schematic front view of optrode, in accordance with one embodiment of the invention;

FIG. **3***b* is a schematic side view of the optrode of FIG. **3***a*, in accordance with one embodiment of the invention;

FIG. **4** is a schematic front view of an optrode transmitting light through cortical neural tissue, in accordance with one embodiment of the invention;

FIG. **5** is a schematic front view of paths corresponding to the travel of light around a pair of optrode shanks, in accordance with one embodiment of the invention;

FIG. **6** is a schematic perspective view of optical and electrical connections for an optrode system, in accordance with one embodiment of the invention;

FIG. **7** is a schematic perspective view of optical and electrical connections for an optrode system, in accordance with one embodiment of the invention;

FIGS. **8***a* through **8***g* are schematic cross-sectional views of a method of manufacturing an optrode, in accordance with one embodiment of the invention;

FIG. **8***h* is a schematic top view of an optrode produced by the method of FIGS. **8***a* through **8***g*, in accordance with one embodiment of the invention;

FIGS. **9***a* through **9***g* are schematic cross-sectional views of a method of manufacturing an optrode, in accordance with one embodiment of the invention; and

FIG. **9***h* is a schematic top view of an optrode produced using the method of FIGS. **9***a* through **9***g*, in accordance with one embodiment of the invention.

DESCRIPTION

It is contemplated that devices, systems, methods, and processes of the claimed invention encompass variations and adaptations developed using information from the embodiments described herein. Adaptation and/or modification of the devices, systems, methods, and processes described herein may be performed by those of ordinary skill in the relevant art.

Throughout the description, where devices and systems are described as having, including, or comprising specific components, or where processes and methods are described as having, including, or comprising specific steps, it is contemplated that, additionally, there are devices and systems of the present invention that consist essentially of, or consist of, the recited components, and that there are processes and methods according to the present invention that consist essentially of, or consist of, the recited processing steps.

It should be understood that the order of steps or order for performing certain actions is immaterial so long as the invention remains operable. Moreover, two or more steps or actions may be conducted simultaneously.

The mention herein of any publication, for example, in the Background section, is not an admission that the publication serves as prior art with respect to any of the claims presented herein. The Background section is presented for purposes of clarity and is not meant as a description of prior art with respect to any claim.

Various embodiments of the present invention feature an optrode probe for optically and/or electrically stimulating and/or recording neural tissue. The optrode may include a plurality of prongs or shanks configured to be inserted or implanted into neural tissue, such as skin tissue, brain tissue, or spinal tissue. Light and electricity may be transmitted through the shanks, and the optical and electrical response of the neural tissue between or around the shanks may be detected by the optrode and analyzed. In certain embodiments, the optrode is used to provide optical and/or electrical stimulation and neural monitoring in clinical applications (e.g., treatment of Parkinson's disease, epilepsy, depression, obesity, hypertension) and/or in research applications (e.g., treatment and/or diagnosis).

FIG. **1** depicts one embodiment of an optrode system **100** that includes a light source **102**, an optrode **104**, and a photo-detector **106**. The light source **102** may include any light generation source, such as a laser, a laser diode, a vertical cavity surface-emitting laser (VCSEL), a light emitting diode, a fluorescent bulb, or an incandescent bulb. The light source may be, for example, an internal light source (i.e., located within the optrode **104**) or an external light source (i.e., located outside the optrode **104**). A pulse modulator **108** may be used to deliver a specified pattern of light pulses or other variations from the light source **102**. Typical wavelengths generated by the light source **102** are visible to near-infrared (e.g., from about 400 nm to about 1000 nm). As depicted, the light source **102** is connected to the optrode **104** using one or more external waveguides **110** and waveguide couplers **112**. Light from the light source **102** travels through the one or more external waveguides **110** and waveguide couplers **112** into the optrode **104**. The optrode **104** includes one or more internal waveguides **114** to direct the light into a transmitting shank **116** of the optrode **104**. The transmitting shank **116** includes one or more apertures **118**, which receive the light from the internal waveguides **114** and direct the light into adjacent neural tissue.

In certain embodiments, at least a portion of the light emitted by the apertures **118** of the transmitting shank **116** is transmitted through the tissue and collected by a receiving shank **120** of the optrode **104**. Like the transmitting shank **116**, the receiving shank **120** includes one or more apertures **122** and internal waveguides **124** for collecting the light and transporting it through the receiving shank **120**. One or more waveguide couplers **126** and external waveguides **128** receive the collected light from the internal waveguides **124** and deliver the light to the photo-detector **106**. The photo-detector **106** measures and analyzes the characteristics of the collected light. For example, the photo-detector **106** may determine the intensity and/or the spectrum of the collected light.

In the depicted embodiment, the optrode **104** includes a calibration waveguide **130** to allow light to pass directly from the light source **102** to the photo-detector **106**, without first passing through the neural tissue. The calibration waveguide **130** enables the photo-detector **106** to directly view the light from the light source **102** and thereby account for variations in the light that may occur over time (e.g., due to drift or power variations). In alternative embodiments, a calibration waveguide is formed as a bifurcation of an internal waveguide. For example, the internal waveguide **114** receiving light from the light source **102** may include a bifurcation or branch that travels directly to the waveguide coupler **126** connected to the photo-detector **106**.

In certain embodiments, light from the light source **102** is directed into the optrode **104** using one or more lenses (e.g., a spherical lens, a biconvex lens, and/or a plano-convex lens) to collect and/or focus the light. The one or more lenses may be incorporated, for example, into one or more of the waveguides and/or waveguide couplers **112**, **126**. In one embodiment, a butt coupling is used to couple the light source **102** and the optrode **104**. Any suitable coupling may be used to direct light from the light source **102** into the optrode **104**.

In certain embodiments, the apertures **118**, **122** and/or internal waveguides **114**, **124** include a light directing element that directs light away from the transmitting shank **116** (e.g., in a direction perpendicular to a longitudinal axis of the transmitting shank **116**). The light directing element may include one or more components that refract, reflect, focus, scatter, and/or perform any suitable manipulation of light. For example, the light directing element may include a reflector (e.g., a mirror) and/or a lens. The lens may be used to focus light to a point away from the transmitting shanks **116**, **120**. In one embodiment, the lens has a focal length preselected to focus light on targeted tissue or on the receiving shank **120**. The focal length may be adjustable and/or variable to enable the lens to focus light at an adjustable distance away from the transmitting shank **116**, thereby providing an improved ability to target particular tissue locations.

In various embodiments, the light directing element includes or is a diffuser. The diffuser scatters the light in all or several directions or angles when the light exits the transmitting shank **116**. The diffuser may include, for example, a collection of particles dispersed in a medium (e.g., a glue or polymer). The diffuser may be a frost coating or covering.

In some embodiments, the optical components (e.g., the apertures **118**, **122** and/or internal waveguides **114**, **124**) of the optrode **104** include a filter that allows only particular wavelengths of light to pass. For example, in some embodiments it may be desirable to interrogate neural tissue with a certain color or wavelength. A filter allowing that color or wavelength to pass may be utilized in this instance to achieve the desired interrogation.

In various embodiments, the optical components of the optrode **104** are selected and configured to transmit light into and/or receive light from the neural tissue. The light source **102** may be, for example, a vertical-cavity surface-emitting laser (VCSEL), such as the VCSEL-780, made by Thorlabs, Inc., of Newton, N.J. Each external waveguide **110**, **128** may be a fiber optic waveguide. The waveguide couplers **112**, **126** may include, for example, a V-groove fiber-waveguide coupler, made by Oz Optics, Ltd., of Ottawa, Ontario. In one embodiment, the photo-detector **106** is a spectrometer, such as the HR2000 made by Ocean Optics, Inc., of Dunedin, Fla. The pulse modulator **108** may be, for example, a laser diode driver, such as a Picosecond Light Pulser, made by Hamamatsu Photonics, of Japan.

In certain embodiments, the pulse modulator **108** is used to output light pulses that have a duration from about 1 picosecond to about 1 millisecond. For example, the duration of the pulses may be from about 1 nanosecond to about 100 nanoseconds. The light pulses may be intensity modulated (e.g., with a modulation frequency from about 50 MHz or less to about 1 GHz or more). The light pulses may have any shape, including, for example, square, triangular, saw-tooth, ramped up, or ramped down.

In some embodiments, the light from the light source **102** is not pulsed. For example, a continuous wave light may be used for steady-state recordings. In such instances, the pulse modulator **108** is not used and/or is not included in the optrode system **100**.

As depicted, the optrode system **100** may also include a trans-impedance amplifier **132** (e.g., with positive or negative feedback, bias, and offset circuitry), an analog-to-digital converter **134**, a microcontroller **136**, computer memory **138**, and/or a wireless components **140** (e.g., to achieve a wireless connection). In various embodiments, these items are used to deliver light pulses, collect captured light spectrographically, record or store data, process data (e.g., analyze data received from the optrode **104**), and transmit data wirelessly to a networked device (e.g., a remote personal computer or workstation). Some or all of these items may be incorporated onto a circuit board that interfaces with the optical and electrical components of the optrode **104**. The circuit board may be located, for example, inside the optrode **104** and/or outside the optrode **104**, either partially or completely.

Although not explicitly shown in FIG. **1**, in certain embodiments, the optrode system **100** also includes electrical components for electrically stimulating the neural tissue and/or receiving electrical signals from the neural tissue. The electrical components may include, for example, an electrical power source, at least one electrode in one or both of the transmitting shank **116** and the receiving shank **120**, and/or a voltmeter or other device (e.g., a data acquisition system) for recording and/or measuring electrical signals received from the neural tissue. In one embodiment, the power source provides a voltage between two or more electrodes. Like the optical input, the electrical input from the power source may be pulsed or modulated over time.

FIG. **2** is a schematic front view of the optrode **104** inserted into a sample of neural tissue **200**, in accordance with one embodiment of the invention. The neural tissue **200** includes microglia **202**, astrocytes **204**, and cortical blood vessels **206**. As depicted, the transmitting shank **116** and the receiving shank **120** include a plurality of internal waveguides **114**, **124** and apertures **118**, **122** for transmitting and/or receiving light. The transmitting shank **116** includes two internal waveguides **114** and two apertures **118**, which direct light into the neural tissue **200** towards the receiving shank **120**. The receiving shank **120** includes two corresponding internal waveguides **124** and apertures **122** for receiving light from the tissue **200** and transmitting the light to the photo-detector **106**. In the depicted embodiment, the transmitting shank **116** and the receiving shank **120** also include a plurality of electrode sites or electrodes **208**. The electrodes **208** are used to stimulate the tissue **200** and/or record electrical signals received from the tissue **200**. Recording may be performed with or without optical or electrical stimulation. In one embodiment, an electrode **208** in one shank (e.g., the transmitting shank **116**) is connected to a power source or a recording amplifier, while an electrode **208** in the other shank (e.g., the receiving shank **120**) is connected to ground or a recording amplifier. A voltage difference between the two shanks **116**, **120** may be detected and recorded.

The optrode shanks **116**, **120** may be made of any solid material that provides the desired mechanical, electrical, and optical properties. In certain embodiments, the optrode shanks **116**, **120** are made of silicon or a flexible polymer, such as polyimide. The internal waveguides **114**, **124** may include one or more glasses, resins, polymers, and/or semiconductors. For example, the internal waveguides **114**, **124** may include a photodefinable polymer or resin, such as polytetrafluoro-ethylene (TFE), chlorotrifluoro-ethylene (CTFE), acrylic, polypropylene, polybutylene, polyethylene, polystyrene, and polysulfone. In some embodiments, the internal waveguides **114**, **124** include organic materials such as SU-8, Poly(methyl methacrylate) (PMMA), perfluoropolymers, polydimethylsiloxane (PDMS), and parylene, and/or inorganic materials such as silicon dioxide (SiO_2), silicon nitride, silicon oxynitride, and silica.

Referring to FIGS. **3***a* and **3***b*, in certain embodiments, the two shanks **116**, **120** of the optrode **104** are separated by a shank separation distance X and have a rectangular cross-section. The shank separation distance X may be between about 20 microns and about 1000 microns, for example about 100 microns or about 200 microns. The shank separation distance X may be uniform or it may vary from a tip **302** of the shanks **116**, **120** to a base **304** of the shanks **116**, **120**. In the depicted embodiment, the shanks **116**, **120** have a rectangular cross-section with a width W and a depth D that are each between about 10 microns and about 100 microns. The width W of each shank is preferably about 25 microns and the depth D of each shank is preferably about 10 microns. In alternative embodiments, the shanks **116**, **120** may have any cross-sectional shape, including hexagonal, triangular, circular, or oval. A length L of the shanks **116**, **120** may be from about 100 microns to about 3000 microns. In one embodiment, the length L of the shanks **116**, **120** is about 1000 microns. In one embodiment, the shanks **116**, **120** are tapered, narrowing towards the tip **302**, to reduce tissue damage during insertion into the tissue **200**. The optrode **104** may be flexible or rigid.

Referring now to FIG. **4**, the optrode **104** includes, in one embodiment, three apertures **118** on the transmitting shank **116** and three apertures **122** on the receiving shank **120**. During operation of the optrode **104**, light exits the apertures **118** on the transmitting shank **116**, passes through the neuronal tissue **200**, and is collected by the apertures **122** on the receiving shank **120**. The configuration allows the optrode **104** to sense changes in tissue morphologies between the two shanks **116**, **120**. For example, as scar tissue accumulates in the tissue **200** over time, the amount of light received by the receiving shank **120** may change.

In certain embodiments, an optrode features a reflectance configuration where source and collection apertures are located on a single shank. For example, a shank may include an aperture for transmitting light into the tissue and an aperture for receiving light reflected by the tissue. Some combination of transmittance and reflectance is also possible. For example, depending on the configuration of the waveguides and apertures, the light received by a shank may come from both the same shank (i.e., reflectance) and a different shank (i.e., transmittance). The received light may also come from a source outside of the optrode (e.g., an external light source) and/or be generated within the tissue (e.g., due to fluorescence). For example, in one embodiment, the tissue emits light (e.g., fluoresces) when exposed to light and/or electricity. In some embodiments, the tissue emits electrical signals when exposed to light and/or electricity. The tissue may be genetically modified to achieve a desired electrical and/or optical response to the electrical and/or optical stimulation.

FIG. **5** depicts an optrode **500** and paths corresponding to the travel of light around the optrode **500**, in accordance with certain embodiments of the invention. Each shank **502** of the optrode **500** includes a plurality of internal waveguides **504** and apertures **506** associated with the waveguides **504**. Some of the apertures **506** are arranged on inner surfaces **510** of the shanks **502**. Other apertures **506** are arranged on outer surfaces **512** of the shanks **502**. In general, light emitted by one aperture **506** may be received by any one of the other apertures **506**. For example, light following a path P**1** is emitted from an aperture **506** on one side of a shank **502** and received by a different aperture **506** on the same side of the shank **502**. Similarly, light following a path P**2** is emitted from an aperture **506** on the inner surface **510** of one shank **502** and received by an aperture **506** on the inner surface **510** of the other shank **502**. Further, light following path P**3** is emitted from an aperture **506** on an outer surface **512** of one shank **502** and received by an aperture **506** on an inner surface **510** of the other shank **502**. In various embodiments, light emitted by an aperture **506** is diffused by the adjacent neural tissue in all directions, thereby allowing the light to be received by any other aperture **506** of the optrode **500**.

FIG. **6** is a perspective view of optical and electrical connections for an optrode system **600**, in accordance with certain embodiments of the invention. The optrode system **600** includes an optrode **602**, a printed circuit board **604**, a waveguide coupler **606**, and an electrical connector **608**. Light is delivered to and from the optrode **602** using the waveguide coupler **606** and an optical cable **610**. The waveguide coupler **606** includes a fixed portion **612** that is butted up against the optrode **602**. An alignment block **614** aligns the internal waveguides of the optrode **602** with the fixed portion **612** of the waveguide coupler **606**. The waveguide coupler **606** also includes a detachable portion **616** that may be disconnected from the fixed portion **612**, as shown. Alignment pins **618** on the detachable portion **616** ensure the detachable portion **616** and the fixed portion **612** are properly aligned when connected.

Electrical power and/or signals are transmitted to and from the optrode **602** using the electrical connector **608** and an electrical cable **620**. The electrical connector **608** may be connected or disconnected from a receptacle (not shown) on the printed circuit board **604**. Contacts **622** on the optrode **602** and/or on the printed circuit board **604** allow electricity to be transmitted between the optrode **602** and the printed circuit board **604**. A head mount **624** allows the optrode system **600** to be fixed or attached to an object, such as an animal.

FIG. **7**. is a perspective view of optical and electrical connections for an optrode system **700**, in accordance with certain embodiments of the invention. The optrode system **700** includes an optrode **702**, a printed circuit board **704**, a waveguide coupler **706**, and an electrical connector **708**. Light is delivered to and from the optrode **702** using the waveguide coupler **706** and an optical cable **710**. The waveguide coupler **706** may be a V-groove optical interface coupler, which may be detachable. Electrical power and/or signals are transmitted to and from the optrode **702** using the electrical connector **708** and an electrical cable **712**. The electrical connector **708** may be connected or disconnected (as shown) from a clip **714** attached to the printed circuit board **704**. Contacts **716** on the optrode **702** and/or printed circuit board **704** allow electricity to be transmitted between the optrode **702** and the printed circuit board **704**. In one embodiment, contacts **716** on the optrode **702** are wire-bonded to the printed circuit board **704**. A head mount **718** allows the optrode system **700** to be fixed or attached to an object, such as an animal.

In certain embodiments, a method of manufacturing an optrode includes embedding internal waveguides and electrodes into shanks of the optrode using photolithographic techniques. For example, in one embodiment, an optrode fabrication process begins with a silicon on insulator (SOI) wafer. The SOI wafer may include a silicon device layer on the order of 20 microns thick, bonded to a silicon handle wafer with an oxide layer. A lower cladding layer of a low index optical polymer may be spun on the SOI wafer and then cured. A high index core layer may then be spun on top of the cladding layer. In certain embodiments, the internal waveguides are defined using a photolithographic process and/or a photolithographic plus etch process. End facets and/or turning mirrors may not be fabricated at this time. A lower index polymer for the upper cladding may then be spun on, possibly in several steps, until a planar surface is created that is sufficiently higher than the core layer. Next, a metal pattern may be defined, either by additive or subtractive processes, which will delineate the end facets of the waveguides, any turning mirrors, and an etch of silicon prongs. These features may then be dry etched, and an etch mask may be removed. Lastly, the silicon handle wafer may be dissolved or ground, yielding the silicon shanks or prongs with the internal waveguides. Additional suitable fabrication processes for the internal waveguides may include micro-opto-electro-mechanical systems (MOEMS) processes, microembossing, thermal nanoimprint lithography (NIL), and/or combined nanoimprinting and photolithography (CNP).

FIGS. **8***a* through **8***g* are schematic views of a method of manufacturing an optrode, in accordance with various embodiments of the invention. Referring to FIG. **8***a*, the method begins with a starting substrate **802**, such as a silicon on insulator (SOI) substrate. A thermal oxide insulation layer **804** is then grown on the starting substrate **802** (FIG. **8***b*). Interconnects **806** (e.g., Cr/Au) and electrodes or recording sites **808** (e.g., Ti/Pt) are deposited and patterned using two-step lithography (FIG. **8***c*). A lower cladding layer **810** (e.g., PDMS) is deposited onto the insulation layer **804**, the interconnects **806**, and the recording sites **808** (FIG. **8***d*). A waveguide core **812** made of, for example, polyimide or SU-8 is deposited and patterned over the lower cladding layer **810** and the interconnects **806** (FIG. **8***e*). An upper cladding layer **814** is then deposited onto the patterned waveguide core **812** and the lower cladding layer **810** (FIG. **80**. Finally, the recording sites **808** and bond pads **816** are opened (FIG. **8***g*).

FIG. **8***h* depicts an optrode **818** produced by the method. In the depicted embodiment, the bond pads **816** are located on a tab or base portion **820** of the optrode **818** while the recording sites **808** are located on a pair of shanks **822** of the optrode **818**. In one embodiment, the bond pads **816** include a gold coating and the recording sites **808** include a platinum or iridium coating.

FIGS. **9***a* through **9***g* are schematic views of another method of manufacturing an optrode, in accordance with various embodiments of the invention. Referring to FIG. **9***a*, the method begins with a starting substrate **902**, such as a silicon on insulator (SOI) substrate (e.g., four inch). A thermal oxide insulation layer **904** is then grown on the starting substrate **902** (FIG. **9***b*). A lower cladding layer **906** (e.g., PDMS) is deposited onto the insulation layer **904** (FIG. **9***c*). A waveguide core **908** made of, for example, polyimide or SU-8 is deposited onto the lower cladding layer **906** (FIG. **9***d*). Next, interconnects **910** (e.g., of Cr/Au) are deposited and patterned (FIG. **9***e*), followed by recording sites **912** (e.g., of Ti/Pt) and bond pads **914** (FIG. **9***f*), and an upper cladding layer **916** (FIG. **9***g*). Finally, as also shown in FIG. **9***g*, waveguide cladding materials **918** are patterned and processed using reactive-ion etching (RIE).

FIG. **9***h* depicts an optrode **920** produced by the method. In the depicted embodiment, the bond pads **914** are located on a tab or base portion **922** of the optrode **920** while the recording sites **912** are located on a pair of shanks **924** of the optrode **920**. In one embodiment, the bond pads **914** include a gold coating and the recording sites **912** include a platinum or iridium coating.

In general, by incorporating both optical and electrical components into the optrode, the optrode advantageously enables optical interrogation and spectroscopy of surrounding tissues with substantially simultaneous electrical recording of neurons and bioimpedance functions. As described above, the waveguide apertures transmit and collect light for optical analysis. Localized apertures and recording electrodes may be used to target specific areas.

In certain embodiments, the optical measurements are used to monitor tissue damage that occurs due to implantation of a probe such as the optrode. For example, insertion of a probe may cause cell death (both glial and neuronal), mechanical tissue compression, a collection of debris resulting from cell death, and severed neuronal processes and blood vessels. Long term implantation of the probe may trigger a foreign body response, primarily affected by microglia and astrocytes. Scar tissue may buildup in the vicinity of the probe. By optically interrogating the neural tissue, the optrode allows the health of the tissue to be monitored over time.

In various embodiments, light received by the photo-detector **106** is analyzed to determine the behavior or health of neural tissue. Analysis techniques that may be utilized include, for example, optical spectroscopy and near-infrared spectroscopy. In some embodiments, a spectroscopic technique includes exposing tissue to different wavelengths of light and evaluating the wavelengths of light received from the tissue. In general, the tissue may absorb or scatter light as a function of wavelength. For example, the tissue may include chromophores that cause one wavelength to be preferentially scattered or absorbed. Based on the spectrum of light received from the tissue, various characteristics of the tissue may be inferred, such as the tissue health, tissue density, and/or a size distribution (e.g., of cells in the tissue).

In some embodiments, the optrode is used to remove scar tissue buildup that has occurred around the optrode. The scar tissue may prevent proper functioning of the optrode by, for example, interfering with the flow of electricity between the tissue and the optrode. In one embodiment, the optrode is used to remove scar tissue by performing optical ablation. The optical ablation may be performed by emitting a high-intensity light (e.g., laser light) from the optrode to burn away adjacent scar tissue. After removing the scar tissue, proper functioning of the optrode may be restored.

In certain embodiments, the optrode is configured to stimulate and record neuron activity both optically and electrically. For example, electrical stimulation and/or optical stimulation may cause an increase, decrease, or block of neuronal activity, and the neural response to the stimulation may be detected and recorded using the electrical components and/or the optical components of the optrode.

Having described certain embodiments of the invention, it will be apparent to those of ordinary skill in the art that other embodiments incorporating the concepts disclosed herein may be used without departing from the spirit and scope of the invention. Accordingly, the described embodiments are to be considered in all respects as only illustrative and not restrictive.

What is claimed is:

1. A transmissive spectroscopic probe, comprising:

a first shank comprising light transmitting optical components disposed within the first shank and configured to transmit light into a sample and towards a second shank of the probe;

the second shank spaced between about 20 microns and 1000 microns away from the first shank and comprising light receiving optical components disposed within the second shank and configured to collect at least a portion of the light transmitted into the sample by the light transmitting optical components; and

electrical components disposed within at least one of the first shank and the second shank for recording an electrical signal from the sample.

2. The probe of claim **1**, further comprising at least one waveguide for transmitting light through the first shank and/or the second shank.

3. The probe of claim **2**, wherein the at least one waveguide comprises a photodefinable polymer.

4. The probe of claim **1**, wherein the light transmitting and light receiving optical components are each in optical communication with at least one aperture defined by the first shank and the second shank.

5. The probe of claim **1**, wherein the electrical components comprise an electrode.

6. The probe of claim **1**, wherein a separation distance between the first shank and the second shank is about 100 microns.

7. The probe of claim **1**, wherein the first shank and the second shank have a width and a depth, each of which is between about 10 microns and about 100 microns.

8. The probe of claim **7**, wherein the width is about 25 microns and the depth is about 10 microns.

9. The probe of claim **1**, wherein the electrical components are further configured to apply a voltage to the sample.

10. The probe of claim **1**, wherein the sample comprises neural tissue.

11. A system, comprising:

a light source;

a probe comprising:

i) a first shank comprising:

light transmitting optical components configured to transmit light into a sample;

ii) a second shank spaced between about 20 microns and 1000 microns away from the first shank and comprising:

light receiving optical components configured to collect light from the sample; and

iii) electrical components disposed within the first shank and the second shank for recording an electrical signal from the sample;

a photo-detector;

a plurality of external waveguides for transmitting light from the light source to the probe and from the probe to the photo-detector; and

a controller configured to spectrographically analyze a light signal collected by the second shank.

12. The system of claim **11**, wherein the electrical components are further configured to apply a voltage to the sample.

* * * * *